

CLAIMS

We claim:

1. A non-human mammal comprising a modified endogenous gene, wherein said endogenous gene is selected from the group consisting of a gene or sequence
5 encoding an ion-channel, a G-protein coupled receptor (GPCR), an immunoglobulin, a growth factor, an enzyme, or a milk protein.
2. A mammal according to claim 1 wherein said mammal is a farm animal.
3. A mammal according to claim 2 wherein said farm animal is selected from the group consisting of cattle, sheep, pigs, horses and goats.
- 10 4. A mammal according to claim 1 wherein said mammal is selected from the group consisting of mice, rats, rabbits , guinea pigs, hamsters and gerbils.
5. A mammal according to claim 1 wherein said milk protein gene is a lactoglobulin gene.
- 15 6. A mammal according to claim 5 wherein said lactoglobulin gene is the α -lactoglobulin gene or the β -lactoglobulin gene.
7. A mammal according to claim 6 wherein said modified α -lactoglobulin gene or β -lactoglobulin gene does not encode any phenylalanine residues.
8. A mammal according to claim 1 wherein said endogenous gene is disrupted by deletion of at least one nucleotide.
- 20 9. A mammal according to claim 1 wherein said endogenous gene is disrupted by an insertion sequence.

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10. A mammal according to claim 9 wherein said insertion sequence is a polylinker sequence.
 11. A mammal according to claim 9 wherein said insertion sequence is a reporter gene.
 - 5 12. A mammal according to claim 11 wherein said reporter gene is selected from the group consisting of a luciferase gene, a β -galactosidase gene and green fluorescent protein (GFP), blue fluorescent protein (BFP), red fluorescent protein (RFP) and yellow fluorescent protein (YFP).
 - 10 13. A mammal according to claim 9 wherein said insertion sequence is selected from the group consisting of a gene encoding human lysozyme, human growth hormone, human serum albumin, human globin, a human immunoglobulin, and a human enzyme.
 14. A mammal according to claim 12 wherein said human enzyme is α -1 antitrypsin.
 - 15 15. A mammal according to claim 12 wherein said human enzyme is anti-thrombin III.
 16. A mammal according to claim 12 wherein said human enzyme gene does not encode any phenylalanine residues.
 - 20 17. A mammal according to claim 9 wherein said insertion sequence is selected from the group consisting of a human gene under control of its endogenous promoter, a modified endogenous regulatory element for an endogenous gene, a transcriptional regulation cassette and a dimerizing sequence.
 18. A mammal according to claim 17 wherein said endogenous regulatory element is disrupted by deletion of at least one nucleotide.

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19. A mammal according to claim 17 wherein said regulatory element is disrupted by an insertion sequence.
 20. A mammal according to claim 1 wherein said enzyme is a sugar transferase enzyme.
 - 5 21. A mammal according to claim 20 wherein said sugar transferase enzyme is α -galactosyl transferase.
 22. A mammal according to claim 21 wherein said α -galactosyl transferase gene is disrupted by deletion of at least one nucleotide.
 - 10 23. A mammal according to claim 21 wherein said α -galactosyl transferase gene is disrupted by an insertion sequence.
 24. A mammal according to claim 23 wherein said insertion sequence is a hormone receptor gene.
 25. A mammal according to claim 23 wherein said insertion sequence is a viral receptor gene.
 - 15 26. A mammal according to claim 23 wherein said insertion sequence is a G-protein coupled receptor gene.
 27. A primate comprising a modified endogenous gene.
 28. A primate according to claim 27 wherein said endogenous gene is disrupted by deletion of at least one nucleotide.
 - 20 29. A primate according to claim 27 wherein said endogenous gene is disrupted by an insertion sequence.

30. A primate according to claim 29 wherein said insertion sequence is a human therapeutic gene.
31. A primate according to claim 29 wherein said insertion sequence is a human antibody gene.